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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/646,778	09/22/2000	Thomas Specht	SCH-1768	7796
23599	7590	12/18/2003	EXAMINER	
MILLEN, WHITE, ZELANO & BRANIGAN, P.C. 2200 CLARENDON BLVD. SUITE 1400 ARLINGTON, VA 22201			LIU, SAMUEL W	
			ART UNIT	PAPER NUMBER
			1653	

DATE MAILED: 12/18/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/646,778

Applicant(s)

SPECHT ET AL.

Examiner

Samuel W Liu

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 11 September 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,4-24,26-29 and 31-51 is/are pending in the application.
- 4a) Of the above claim(s) 1, 4-23,26,28-29, 31-34 and 36-41 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 24,27,35 and 42-51 is/are rejected.
- 7) ☒ Claim(s) 24 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 13) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
- a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

Applicants' amendment filed 11 September 2003, which cancels claims 2-3, 25 and 30, amends claims 24 and 27, and adds claims 42-51 has been entered. Also, applicants' request (filed 11 September 2003) for extension of time of three months has been entered. The following pending claims 24, 27, 35 and 42-51 are examined in this Office action.

Please note that grounds of objection and/or rejection not explicitly restated and/or set forth below are withdrawn.

Objection to claims/specification

The disclosure is objected to because of the following informalities:

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code in page 142, lines 4 and 7. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

In claim 24, "SEQ ID NOS:" should be change to "SEQ ID NOs:".

Appropriate correction is required.

Claim Rejections - 35 USC § 101

35 U.S.C. §101 states:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title.

Claims 24, 27, 35 and 42-51 are rejected under 35 USC 101 because the claimed invention is not supported by either a specific and substantial credible utility or a well-established utility.

The claimed polypeptide is not supported by a *specific asserted utility* because (i) the disclosed polypeptide is not actually characterized but rather predicted via analyzing database (e.g., LifeSeq database – EST libraries), (ii) pharmaceutical use of the polypeptide relies on electronic Northern Blot, i.e., a contemplative analysis of the data from the databases, (iii) expression of the polynucleotide (SEQ ID NO:265) that encodes SEQ ID NO:288 polypeptide does not have tissue specificity as it also overexpress in normal tissue, e.g., seminal vesicle (see page 130, and (iv) the expression pattern shown in page 130 in normal ovary and ovarian tumor tissue are indistinguishable.

The specification sets forth use of the claimed polypeptide subsequence (i.e., the partial sequence), the fragment possessing 90% sequence identity to SEQ ID NO:288, to identify composition against cancer, i.e., treating cancer disorder state (see page 7, the fourth paragraph). However, there is neither working examples nor guidance as to how to make and use it in the specification regarding the claimed subsequence; the specification only provides evidence for algorithm of identifying cDNA encoding the polypeptide SEQ ID NO:288 with altered expression using tissue-specific electronic Northern Bolt (see Example 2). Note that electronic Northern blot does not represent reasonable establishment in reducing the invention to practice, but rather a contemplation of the claimed composition. Thus, there is no specific utility and substantially utility associated with the claimed protein.

Also, the specification as filed does not provide experimental evidence that points to an activity (biological role or/and therapeutic role) of the polypeptide SEQ ID NO:288. Additionally, there is no art of record that discloses or suggests any activity for the claimed polypeptide. Thereof, there is no substantial utility associated with the polypeptide.

The specification sets forth that the invention relates to pharmaceutical agent containing the claimed polypeptide (see page 7, the last two lines). Yet, nowhere in the specification describes factual evidence in this regard, e.g., provides animal model or experimental data to support what is claimed.

The specification sets forth that the claimed polypeptide can be use as pharmaceutical agent for treating ovarian cancer (see page 7, the paragraphs 4-6, and claim 35). The specification appears to correlate candidate genes that is EST-database orientated as well as tumor-related (see Example 1) with the claimed composition based on the altered mRNA expression pattern of the genes (see Example 2). Such the apparent correlation does not establish the specific utility of the current disclosure. As yet, it has been widely accepted that the actual steady state level of mRNA molecules, is not well correlated with the actual protein abundance (see Aebersold, R. et al. (2000) *Annals of the New York Academy of Sciences* 919, 33-47). Moreover, numerous proteins undergo *up* or *down* cellular regulation responsive to the extracellular signals and intracellular signaling (*i.e.*, cell signaling pathways cross-talk), which dramatically regulate mRNA expression of polypeptide. Since the examples set forth in the specification does not suffice establishing the anti-tumor activity of the claimed polypeptide, and since even the results from theoretical analysis, *i.e.*, electronic Northern Blotting (see page 130) shows no specificity of the claimed polypeptide in view of comparison of normal tissue tissues or comparison of normal ovary with ovarian tumor tissue. Thus, there is no specific and asserted utility or well-established utility associated with the claimed polypeptide.

After further search, a specific and substantial credible utility might be found for the claimed isolated compositions. This further characterization, however, is part of the act of the

invention and until it has been undertaken, applicants' claimed invention is incomplete. The current disclosure is therefore deemed lack of specific and substantial utility or well-established utility.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 24, 27, 35 and 42-51 are also rejected under 35 U.S.C. 112, first paragraph. Specially, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reason set forth above, one skilled in the art would not know how to use the claimed polypeptide so that it would operate as intended without undue experimentation. This rejection stands for the reasons set forth in the foregoing statement of the grounds of rejection under 35 U.S.C. 101.

Claims 24, 27, 35 and 42-51 are rejected under 35 U.S.C. 112, first paragraph, because the specification, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant is not in possession of the claimed polypeptide and subsequence that is 90% sequence *homology* to SREQ ID NO:288 (see claim 44) and a fragment thereof (see claim 51), and a pharmaceutical composition comprising the polypeptide or/and subsequence thereof.

The instant claim language appears to encompass numerous subsequences since “sequence homology” and “fragment” would include substitution, insertion deletion of the full-length polypeptide SEQ ID NO:288; the resulted variants or subsequences would be enormous and unpredictable in structure and function whereas the specification does not provide sufficient description in this regard. The recitations of “sequence homology” and “fragment” do not require that the full-length sequence set forth in SEQ ID NO:288; but rather encompasses any amino acid sequence comprising either the SEQ ID NO:288 or any subsequence. Thus, it would require undue experimentation for the skilled artisan to determine which subsequences of SEQ ID NO:288 would have the function of the full length molecule to facilitate protein of interest folding and increase solubility thereof.

One of skill in the art would reasonably conclude that the disclosure insufficiently provides written description regarding the biological activity or role(s) of the claimed polypeptide and fragments (*i.e.*, subsequences). The specification provides insufficient teaching, guidance and no working examples as to make and use of the protein in diagnosing ovarian tumor. Thus, Applicant was not in possession of the pharmaceutical composition comprising the claimed polypeptide and the fragments thereof. *See University of California v. Eli Lilly and co.* 43 USPQ2d 1398.

Description of invention's reduction to practice, unaccompanied by any meaningful, distinguishing characteristics of evolved the polypeptide variants, *i.e.*, subsequence fragments, is insufficient to satisfy written description requirement of 35 U.S.C. §112, since inventors could have provided description of claimed portion of SEQ ID NO:288, since actual reduction to practice may demonstrate possession of embodiment of invention, but it does not necessarily

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describe what invention is, and since, in context of present case, disclosure of manner in which invention was reduced to practice does not satisfy more fundamental written description requirement set forth in Section 112.

Claim 51 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The specification as originally filed does not provide support for the invention as now claimed.

This is a New Matter rejection for the following reasons:

The newly added claim 51, "a specific fragment" represents a departure from the specification and the claims as originally filed.

The instant claim recites limitation "a specific fragment" which were not clearly disclosed in the specification and claims as filed, and now change the scope of the instant disclosure as filed. Such limitations recited in the present claims, which did not appear in the specification or original claims, as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C. 112.

The response to the rejections under 35 USC 101 and 112, the first paragraph

The response filed 11 September 2003 argues that the polynucleotide (SEQ ID NO:265) encoding the claimed polypeptide (SEQ ID NO:288) can be used as diagnostic markers as indicated in page 1, page 4, lines 1-3 and page 14, and that, as shown in pages 130 and 159, the

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expression of SEQ ID NO:265 is higher in ovarian tumor than in normal ovary (see page 9 of the response). The applicants' argument is found unpersuasive because of the reasons set forth in the above rejections and the following reasons. The current application is directed to polypeptide NOT a polynucleotide encoding the claimed polypeptide. Pages 1 and 14 of the specification do not indicate SEQ ID NO:288 can be used as the diagnostic marker for ovarian tumor. Page 4, lines 1-3 of the specification recites that polynucleotides SEQ ID NOs: 258-273 are expressed elevated in ovarian tumor tissue. However, pages 130 and 159 of the specification show no distinguishable results between normal ovary and ovarian tumor tissues (e.g., expression in normal tissue –seminal vesicle also is higher comparable to the expressed level in ovary or ovarian tumor tissue). Thus, there is not specific and asserted utility associated with the claimed polypeptide.

The response asserts that the submitted figure exhibits over-expression of SEQ ID NO:288 polypeptide (also known as "AGR2") in ovarian tumor compared to expression the same in normal ovarian tissue (see the bridging pages 9-10). The applicants' argument is not persuasive because the polynucleotide encoding SEQ ID NO:288 also over-expresses in normal tissue (see the above statement).

Further, applicants argue that the specific fragment of SEQ ID NO: 288 (note the response contains the typo-errors (i.e., SEQ ID NO:268 (288); see claim 50 (51)) can be identified via searching algorithms or via nucleotide sequences (BLAST) databases and that 90% sequence homology can be identified and manufactured by the skilled artisan (see page 11). The applicants' argument is unpersuasive because of the reason set forth in the above rejection under 35 USC 112, the first paragraph. The recited fragment and the sequence homologs represent a

genus encompassing numerous subsequence or variants which structural and function are unpredictable (see the foregoing statement); thus, required is undue experimentation. The instant disclosure needs to provide sufficient evidence to support a description that a disclosure does not satisfy the enablement requirement.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 24, 27, 35, 44-47 and 49-50 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 24 and 35 recite the non-elected sequences of SEQ ID NOs: 124-257, 274-287 and 189-307 which are patentably distinct from the elected sequence SEQ ID NO: 288 and drawn to non-elected invention. Such the recitation renders the claims indefinite. Thus, re-writing the claim is advised in order to eliminate the subject matters which have been withdrawn from consideration in this Office Action.

Claim 27 recites "...is capable of binding ..."; wherein the recitation "capable of" renders the claim indefinite, since it does not equate to indication the specific binding must actually occur.

Claim 44 is indefinite because the recitation "amino acid sequence having at least 90% sequence homology to ..." is unclear as to whether or not amino acid sequence *homology* refers

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to sequence *identity* or/and structural/functional *similarity*, e.g., substitution of threonine with serine residue would result in the sequence *similarity (homology)*, and, as to whether or the said homology refers to protein structural homolog, i.e., secondary structure similarity or ternary structure similarity. The dependent claims are also rejected.

The previous claim Rejections - 35 USC § 102 is withdrawn in view of the applicants' cancellation of the rejected claim 2.

Provisional Rejection, 35 U.S.C. 101, Double Patenting

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title.

A rejection based on double patenting of the “same invention” type finds its support in the language of 35 U.S.C. 101 which states that “whoever invents or discovers any new and useful process... may obtain a patent therefor...” (Emphasis added). Thus, the term “same invention,” in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

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Claims 42 and 44 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 23 and 26 of copending application No. 09674266, respectively (note that SEQ ID NO:181 of the 09674266 is identical to SEQ ID NO:288 of the instant application). This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

Provisional Rejection - Obviousness Type Double Patenting

Claims 24 of this application conflict with Claims 23, 26 and 32 of Application No. 09674266. 37 CFR 1.78(b) provides that when two or more applications filed by the same applicant contain conflicting claims, elimination of such claims from all but one application may be required in the absence of good and sufficient reason for their retention during pendency in more than one application. Applicant is required to either cancel the conflicting claims from all but one application or maintain a clear line of demarcation between the applications. See MPEP § 822.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the “right to exclude” granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground

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provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130 (b). Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 24, 26, 35, 42-44, 46 and 51 are provisionally rejected under the judicially created doctrine of double patenting over claims 23, 26, 32 and 43 of copending Application No. 09674266. This is a provisional double patenting rejection because the conflicting claims have not in fact been patented.

The subject matter claimed in the instant application is fully disclosed in the referenced copending application and would be covered by any patent granted on that copending application since the referenced copending application and the instant application are claiming common subject matter, as follows:

Claim 23 of Application 09674266 discloses the polypeptide (SEQ ID NO:181) that is identical to the polypeptide (SEQ ID NO:288) disclosed in the instant application; thus, the claim is obvious variation of claims 24 and 42-43 of the current application.

Claim 26 of Application 09674266 sets forth the claimed polypeptide is at least 90% homologous to the SEQ ID NO:181. Thus, claim 26 of 09674266 and the application claims 26, 44 and 46 disclose the common subject matter.

Claim 32 of Application 09674266 and claim 35 of the current application disclose the common subject matter, *i.e.*, a pharmaceutical composition comprising the claimed polypeptide.

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Claim 43 of 09674266 discloses an isolated polypeptide consisting of SEQ ID NO:181 that is identical to SEQ ID NO:288 of the instant application; thus, claim 43 is an obvious variation of claim 51 of the current application.

Therefore, the instant application and Application 09674266 claims are obvious variation, and they are not patentably distinct from each other.

It is noted that page 12 of the response filed 11 September 2003 requests abeyance of the obvious-type double patenting rejection until allowable subject matter is indicated. Note that no allowable subject matter can be indicated with a standing ground of rejection. Thus, it is suggested that applicant file the appropriate terminal disclaimer.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be

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calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

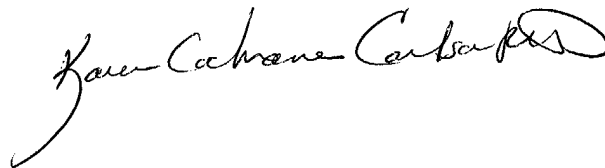
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Samuel Wei Liu whose telephone number is (703) 306-3483.

The examiner can normally be reached from 9:00 a.m. to 5:30 p.m. on weekdays. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Christopher Low, can be reached on 703-308-2923. The fax phone number for the organization where this application or proceeding is assigned is 703 308-4242 or 703 872-9306 (official) or 703 872-9307 (after final). Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703 305-4700.



Samuel Wei Liu, Ph.D.

December 1, 2003



KAREN COCHRANE CARLSON, PH.D.
PRIMARY EXAMINER